ion, not just an academic discussion, because the role of rs8099917 has been clarified and deepened in several studies and we think it should be included as best SVR predictor in the genotype 1 [2–4]. The major impact of rs12979860 has been documented on the early response [5], while rs8099917 in a recent meta-analysis evidenced the best predictive effect on the SVR (OR = 5.171 *vs.* 4.473) [6]. In fact, the effect of this SNP explains the higher rate of relapse in patients who achieved both RVR and ETR with the CC rs12979860 genotype, but with the presence of a G allele for the rs8099917 SNP [5]. Conversely, patients without the CC genotype for rs12979860 retain good probability to reach SVR if they have the TT genotype for rs8099917; this issue could underlie the high rate of SVR in non-CC patients reported by Andriulli *et al.* [1] and according with the TT prevalence in the Italian population. Therefore, we consider it essential to get both rs12979860 and rs8099917 SNPs as predictors on SVR and, in more detail, we could select the patients with CC/TT or CT/TT, but not with CC/TG or CC/GG genotype, for dual therapy.

Another not considered issue in the analysis is the role of therapeutic drug monitoring (TDM) of ribavirin (RBV) as useful early on treatment predictor of response and toxicity. Ribavirin shows a wide inter-individual variability in plasma concentrations (~25–30%) and weight-based dose results often inadequate without TDM support [3,4,7]. Interestingly, RBV concentrations are related both with EVR and SVR [3,4,8,9] or treatment failure in HCV-1 infected patients, according to different plasma concentrations at different time-points. The optimal therapeutic range of RBV could maximize the SVR achievement and it should be comprised between 2–2.5 mg/L (at week 4 of therapy), according to the majority of the reviewed studies [10].

In conclusion, we suggest that both *IL28B* SNPs should be considered in order to refine the selection of candidate patients for dual therapy and then the TDM of RBV should be used to improve the on-treatment management.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Reply to "Triple or dual therapy for HCV-1 naive patients? Optimizing selection tools"

To the Editor:

We thank Dr. Boglione and colleagues [1] for their comments on our recently published paper on the identification of naïve HCV-1 patients with chronic hepatitis who may benefit from dual therapy with peg-interferon (PegIFN) and ribavirin (RBV) [2]. To date, several single nucleotide polymorphisms (SNPs) in the genes encoding for IFN-λ1 (*IL29*), IFN-λ2 (*IL28A*), IFN-λ3 (*IL28B*), and IFN-λ4 (*IFNL4*) have been established as predictors of treatment response to PegIFN/RBV [3,4]. Among the identified SNPs, rs8099917, rs12979860, and the newly ss469415590 polymorphisms have been extensively investigated. Although with conflicting results, the question about which of the aforementioned SNPs, alone or in combination, is (or are) the best baseline marker(s) of SVR in patients HCV1 is still debated.

Dr. Boglione *et al.* argue that the contemporary evaluation of the two SNPs of the *IL28B* locus may portend greater information

Table 1. Genotypes distribution of rs12979860 and rs8099917 SNPs in *IL28B* locus and Sustained Virological Response (SVR).

	rs12979860					
	CC	SVR (%)	CT	SVR (%)	TT	SVR (%)
rs8099917						
GG	0	0 (0)	3	0 (0)	33	7 (21)
TG	15	7 (47)	208	62 (30)	42	10 (24)
TT	104	74 (71)	118	39 (33)	16	5 (16)

on the actual outcome of therapy, as the rs12979860 could better predict RVR, whereas the rs8099917 would be more informative for SVR. We addressed this point in a subsequent manuscript where 539 patients of the entire cohort, for whom blood samples were available, were genotyped for the two SNPs [5]. In our patients the rs12979860 resulted to have a greater impact of the rs8099917 for either RVR (OR = 4.69, 95% CI 3.00–7.34 *vs.* OR = 3.01, 95% CI 1.97–4.59) and SVR (OR = 5.15, 95% CI 3.32–7.98 *vs.* OR = 2.46, 95% CI 1.72–3.51). Moreover, we entered the two SNPs together with the new ss469415590 dinucleotide variant (located in *IFNL4* gene) into a multiple logistic model and the hit SNP appeared to be the rs12979860CC genotype, as it was the only one to retain an independent prediction power for SVR (OR = 3.39; 95% CI 1.61–7.13). The discrepancy between our data and the referenced results by Stättermayer *et al.* [6] could be explained by differences in the HCV genotypes between patients enrolled into the two studies: while our data refer to only patients with HCV-1, the Stättermayer cohort of patients was a mix population of patients infected by all HCV genotypes.

A further point raised by Dr. Boglione concerns the capability of predicting SVR in patients with the rs12979860 non-CC type by determining the TT genotype of the rs8099917. In the accompanying Table 1, we stratified our patients by both genotypes: of the 420 individuals with non-CC type, SVR rates were documented in 33% (44/134), 29% (72/250), and 19% (7/36) of subjects with the rs8099917 subtypes TT, TG or GG, respectively.

While we may agree with our colleagues that monitoring of ribavirin levels during therapy could also impact positively on the outcome of therapy, we have not considered this point in our work.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Virtual portal pressure from anatomic CT angiography

To the Editor:

We read with great interest the paper "Accurate computed tomography-based portal pressure assessment in patients with hepatocellular carcinoma", which proposed a novel CT-based model in the prediction of hepatic venous pressure gradient (HVPG) [1]. By combining liver/spleen volume ratio and the presence of peri-hepatic ascites, this non-invasive model had a very good accuracy in predicting HVPG >10 mmHg [1]. Although HVPG